Exhibit D

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UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

SAN FRANCISCO DIVISION

GUARDANT HEALTH, INC.,

Plaintiff and Counterclaim-Defendant,

vs.

NATERA, INC.,

Defendant and Counterclaim-Plaintiff.

CASE NO. 3:21-CV-04062-EMC

SUPPLEMENTAL EXPERT REPORT OF HOWARD S. HOCHSTER, M.D.

Judge: Honorable Edward M. Chen

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I. INTRODUCTION

1. My name is Dr. Howard S. Hochster. I previously submitted an opening expert report in this case entitled "Opening Expert Report of Howard S. Hochster, M.D.," dated August 22, 2022, and a rebuttal expert report entitled "Rebuttal Expert Report of Howard S. Hochster, M.D.," dated September 13, 2022, on behalf of Defendant and Counterclaim-Plaintiff Natera, Inc. ("Natera"). I will refer to my previous reports as my Opening Report ("Op.") and my Rebuttal Report ("Reb."), respectively.

2. I submit this supplemental report to address the latest performance results of Plaintiff and Counterclaim-Defendant Guardant Health Inc.'s ("Guardant") product, Reveal, in the **C**irculating tum**O**r DNA as a Predictive **B**ioma**R**ker in **A**djuvant Chemotherapy in Patients with Stage IIA Colon Cancer ("COBRA") study that was recently published and presented at the 2024 American Society of Clinical Oncology Gastrointestinal Cancers Symposium (more commonly known as "ASCO-GI") in January 2024.

3. The COBRA Study is sponsored by NRG Oncology, which is one of five national cancer cooperative groups funded by the National Cancer Institute (NCI), a government entity. Unlike the Parikh Study, Guardant's employees are not investigators in the COBRA study.[1]

4. In my Opening Report, I noted that the COBRA study was an ongoing clinical trial using the Reveal assay for detecting the persistence of colon cancer after surgical resection in stage II colon cancer using ctDNA.[2] Because the trial was in an early stage at that time, there were no available results for me to discuss. Recently, significant events have occurred for the COBRA study. As I will discuss below, these events further support and confirm my opinions regarding Guardant Reveal, as set forth in my Opening Report, including my concerns regarding its propensity to give false positive results.

[1] Although Guardant supported the study by providing the Reveal test.
[2] Op., ¶ 119

5. I reserve the right to modify or supplement my opinions, as well as the basis for my opinions, in light of any documents, testimony, or other evidence that may emerge during the course of this matter, including additional deposition testimony or newly-produced documents.

II. SUMMARY OF OPINIONS

6. Below I set forth a high-level overview of the opinions I have expressed in this report. This section is for reference only and not intended to be an exhaustive list of all my opinions on any subject.

7. As reported at ASCO-GI, the COBRA study data showed that the Reveal test's performance in the real-world, large-scale prospective randomized trial deviated significantly from the results reported in the Parikh Study and Guardant's representations to oncologists and patients.

8. As a result, the NCI and the NRG required that the COBRA study be closed to further accrual for futility. This was unprecedented in my long experience as an NCI investigator.

9. Based on my understanding of this case, Natera's concerns with Guardant's advertised claims about Reveal were predictive of the assay's problems that were exposed by the COBRA study failure.

III. EXPERIENCE AND QUALIFICATIONS REGARDING THE COBRA STUDY[3]

10. As a Professor of Medicine at Rutgers Cancer Institute and practicing clinical oncologist, I routinely follow clinical trials in the colorectal cancer space, including the COBRA study. I also regularly attend meetings hosted by ASCO, including the ASCO GI Symposium from January 18-20, 2024, where data from the COBRA study was recently presented and discussed.

11. I am very familiar with the COBRA study. I have been monitoring its progress and results since its initiation in 2019. Rutgers Cancer Institute is one of a few NCI-designated Comprehensive Cancer Centers in the country and is committed to participating in NCI clinical trials. Additionally, I direct all GI Oncology research at Rutgers Cancer Institute, and in this role, I

[3] My experience and qualifications are set forth in paragraphs 4-13 of my Opening Report and Exhibit A thereto. My compensation in this matter, previous testimony, and materials considered are also set forth in my Opening Report.

upheld the Institute's commitment by recommending patients who were eligible to participate in the COBRA study.

12. As discussed in my Opening Report, because of the various drawbacks of the design of the Reveal test as compared to tumor-informed tests, I have been skeptical of the performance of the Reveal test and I do not typically prescribe it to my patients in my general practice for MRD testing. I trusted that NCI, as the study's sponsor, and the investigators leading the COBRA study had thoroughly evaluated the ctDNA test they ultimately selected, *i.e*., Guardant's Reveal test. In addition, the study design included a safeguard in the Phase II stopping point on Reveal's performance, which I will explain further below. Based on that assurance from NCI and my colleagues, I recommended to my patients who were eligible that they participate in the COBRA study in 2021 and 2022.

IV. THE SIGNIFICANCE OF THE COBRA STUDY

13. The COBRA study was initiated in 2019 and is a national multi-center randomized Phase II/III clinical trial. Its main goals were "assessing the elimination" (or "clearance") "of circulating tumor DNA (ctDNA) and determining the recurrence-free survival rates in patients who test positive for ctDNA after surgery and receive chemotherapy" in comparison to patients undergoing the current standard-of-care active surveillance.[4]

14. To oncologists, the COBRA study is significant as these physicians are currently evaluating whether ctDNA is a reliable marker for cancer prognosis and whether MRD testing offers a more reliable method for early detection of cancer recurrence than the current standard of care, which estimates recurrence risk based on pathological staging combined with periodic CT scans and conventional blood tests.[5] As I explained in my Opening Report, the accuracy of a test that detects cancer recurrence is critically important to physicians, as the goal is to permit clinical physicians to reliably prognosticate and accurately determine treatment plans for cancer patients, including

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[4] *Guardant Health Close enrolment in COBRA Study Following Interim Analysis*, NS MEDICAL DEVICES (September 4, 2023) https://www.nsmedicaldevices.com/news/guardant-health-closes-enrolment-in-cobra-study-following-interim-analysis/

[5] Op., ¶¶ 35-36.

whether additional chemotherapy is necessary.[6] Therefore, to be clinically useful, the selected ctDNA test must be both reliable and accurate in determining the presence or absence of ctDNA in the blood sample.

15. The ultimate goal of the COBRA study was to use an MRD test to identify which patients among a particular cohort of early stage colon cancer would benefit from chemotherapy. Specifically, patients whose physicians would not generally prescribe adjuvant chemotherapy (*i.e.*, those patients without traditional high-risk features) were eligible to participate in the COBRA study. These patients were mainly in pathological stages T2 or T3 and N0 (no cancer found in regional lymph nodes). Given the relatively low risk of recurrence for this cohort, oncologists do not typically recommend administering adjuvant chemotherapy because it will not be beneficial for the great majority of patients, and it may cause unwanted short-term and long-term health side effects. However, some patients in this cohort, approximately 10%, will actually recur,[7] and chemotherapy would potentially benefit them if we could identify who they are.

16. Initially projected to enroll 1400+ patients,[8] the COBRA study ultimately enrolled approximately 635 patients across hundreds of participating clinics nationwide before it was halted for reasons I discuss below.

A. COBRA Study Design

17. The COBRA study is a true prospective and randomized clinical trial, as opposed to the Parikh Study. Without the benefit of knowing patients' recurrence outcomes, the COBRA study avoids the risk of biasing the results and creates an ideal condition to test the performance of an assay. Data was analyzed and reported independently in parallel across over 400 locations nationwide. No site is aware of the outcome of the rest of the patient population.

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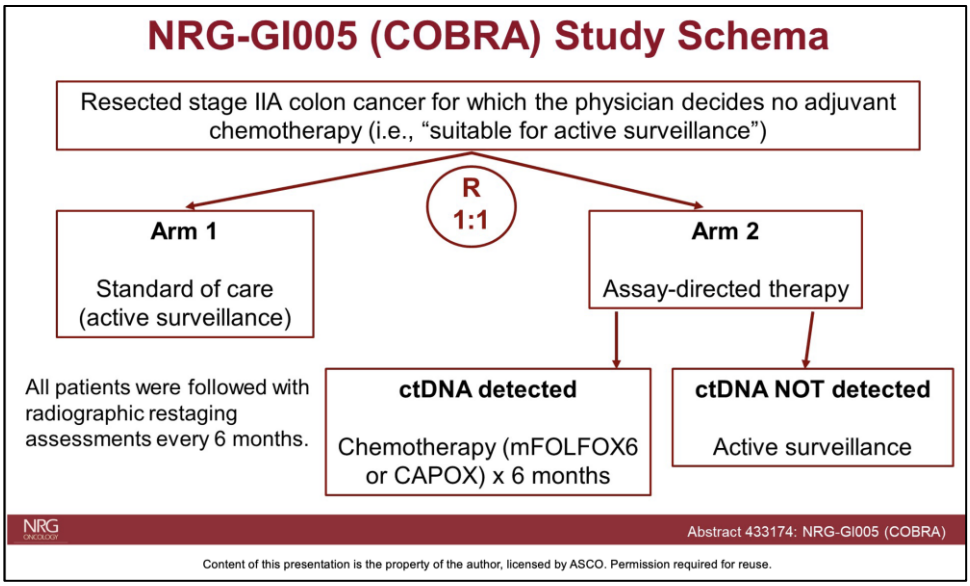
[6] *Id.*, ¶ 39.

[7] As explained in my Opening Report, approximately 10% of the patients in this cohort will relapse after surgery. *See* Op., ¶ 33.

[8] *Circulating Tumor DNA Testing in Predicting Treatment for Patients with Stage IIA Colon Cancer After Surgery*, CLINICALTRIALS.GOV, https://clinicaltrials.gov/study/NCT04068103 (last visited (Jan. 31, 2024).

18. Participants are randomized 1:1 into two arms: standard of care treatment (*i.e.*, observation) vs. prospective ctDNA-assigned treatment.[9] This is illustrated in a slide from Dr. Van Morris's presentation at the 2024 ASCO-GI Conference, which I will discuss in further detail below.[10]



19. For patients in the observation arm ("Arm 1" above), the ctDNA status was analyzed but no study personnel or participants were informed of the result, and patients were observed as per standard of care. For the ctDNA treatment arm ("Arm 2"), postoperative blood samples from each participant were analyzed for the presence or absence of ctDNA using the selected ctDNA test. Participants who test positive for ctDNA in the initial test were then treated with six months of adjuvant chemotherapy. All patients were followed with ctDNA tests and CT scans every 6 months for signs of recurrence.

20. As an early and predetermined checkpoint for the reliability of the ctDNA MRD assay, the COBRA study design mandated a Phase II intermediate endpoint analysis utilizing the

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[9] Ex. 3 (Morris et al, *Phase II/III Study of Circulating Tumor DNA as a Predictive Biomarker in Adjuvant Chemotherapy in Patients with Stage II Colon Cancer*, ASCO-GI Poster TPS3625 (2023) (hereinafter "2023 COBRA Abstract")) https://ascopubs.org/doi/10.1200/JCO.2023.41.16_suppl.TPS3625.

[10] Ex. 1 (Morris et al, *Phase II results of circulating tumor DNA as a predictive biomarker in adjuvant chemotherapy in patients with stage II colon cancer: NRG-GI005 (COBRA) Phase II/III study*, ASCO-GI Presentation Slides (2024) (hereinafter "2024 COBRA Presentation")) at 3.

clearance of ctDNA with adjuvant therapy, as an early stopping rule before moving on to Phase III (which is the larger, more definitive portion of the study based on recurrence free survival for ctDNA-detected patients with or without adjuvant chemotherapy).[11] At this analysis, the patients in both arms who initially tested ctDNA positive (anticipated to be 5%), whether in the observation group or in the treatment group, where the patients will receive adjuvant chemotherapy, would be compared for "clearance" of ctDNA after 6 months of treatment. Comparing the ctDNA clearance rate from both groups, if the ctDNA clearance rate was approximately 50% higher in the treatment arm than in the observation arm, the trial would move on to Phase III.

21. A statistics measurement is also used to determine whether Phase II endpoint is met—p-value. A "p-value" is a statistical measurement used to indicate the statistical significance of the observed differences between two groups. The smaller the p-value, the more likely there is a true difference between the two groups. Typically, to reach what is conventionally considered "statistical significance," the p-value must be less than 0.05 (meaning the same result would be achieved 95 out of 100 times). However, considering the screening nature of the Phase II portion of the COBRA study (with a small number of ctDNA+ patients), the NRG statisticians and clinicians decided that the study would continue even with a p-value of 0.35.[12] That is, the clearance rates would be promising enough to continue even if the study results would be correct only 65 out of 100 times. If the difference in clearance rates had a higher probability of not being different, *i.e.*, p>0.35, "the study would be stopped for futility."[13]

22. Fundamentally, none of the COBRA goals could be achieved if the underlying MRD test was found to be unable to accurately detect the presence or absence of ctDNA. This highlights the importance of having the pre-specified Phase II endpoint as an early check for the fidelity of the ctDNA test. If at the six-month period, the Phase II endpoint study results meet the requirement

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[11] Ex. 2 (Morris et al, *Phase II results of circulating tumor DNA as a predictive biomarker in adjuvant chemotherapy in patients with stage II colon cancer: NRG-GI005 (COBRA) Phase II/III study*, ASCO-GI (2024), https://meetings.asco.org/abstracts-presentations/228849 (hereinafter "2024 COBRA Abstract")).

[12] *Id.*

[13] *Id.*

(p<0.35, *see supra*), the ctDNA test is deemed sufficiently reliable for the trial to move forward with the full Phase III accrual. If, however, the requirement is not met (*i.e.*, p>0.35), the ctDNA test is considered insufficiently reliable for further testing and for the continuation of the trial.[14]

23. Relying on the results reported in the Parikh Study, Guardant's LUNAR (Reveal) test was selected as the ctDNA test for the COBRA study.[15] I understand that the version of the Reveal test used in the COBRA study is the same as the commercial version of Reveal launched in 2021.[16] In other words, the Reveal test used for the COBRA study had both a somatic panel (to detect colon cancer-relevant mutations) and a methylation panel (to detect colon cancer-specific methylation profiling).[17] The COBRA study initially projected that final results would be available in 2027.[18]

B. Early Termination of the COBRA Study

24. On July 5, 2023, NRG announced the suspension of the COBRA study in order to perform the preplanned Phase II endpoint analysis.[19] However, within just two months, the NRG terminated accrual to the study for futility, based on the surprisingly negative Phase II results. NRG and NCI announced that already-enrolled patients would continue to be monitored and be provided follow-up treatment. Letters informing patients of this adverse finding were sent out to all participants by their local institutions.

25. The announcement to shut down the COBRA study shook the field, including myself. The magnitude of the COBRA study failure is unprecedented in my 30 years of experience.

26. The actual data relating to the Phase II endpoint results were not publicly released until January 16, 2024, in one of the abstracts included in the ASCO-GI conference materials. The

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[14] *Id.*

[15] Ex. 1 (2024 COBRA Presentation) at 5.

[16] GHI00006897 at GHI00006915; GHI00050081 at GHI00050087.

[17] *See* Ex. 3 (2023 COBRA Abstract); Ex. 1 (2024 COBRA Presentation) at 5; *see also* Op., ¶¶ 88, 90-91.

[18] *See supra* n.8 (Study Completion (Estimated): 2027-04-30).

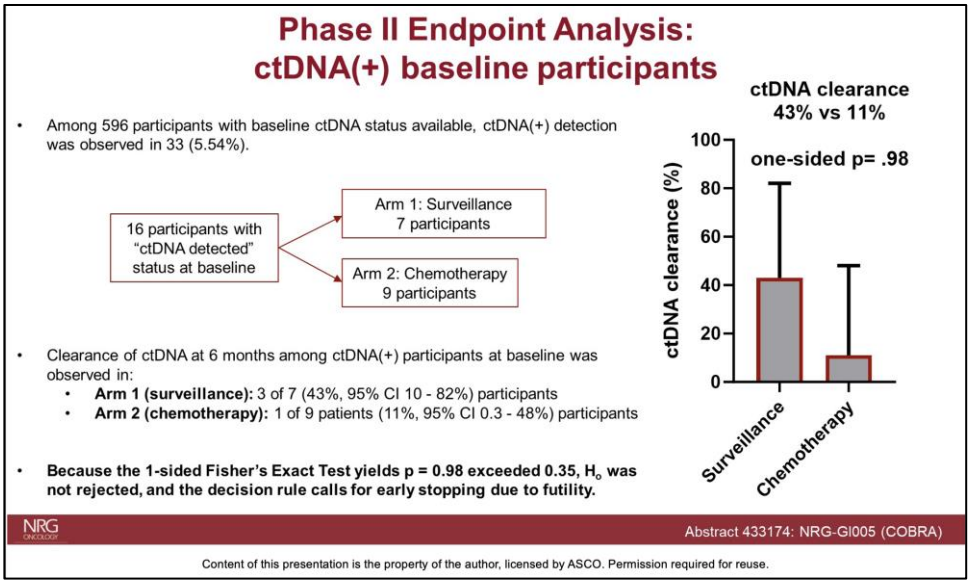
[19] *NRG-GI005 Time Sensitive: Temporary Accrual Suspension*, NRG ONCOLOGY ENEWS, https://myemail.constantcontact.com/Protocol-NRG-GI005--COBRA---Temporary-Accrual-Suspension.html?soid=1139396743412&aid=yt0T_c54JJA (last visited Jan. 31, 2024).

results were presented in an oral session during the ASCO-GI 2024 conference on January 20, 2024. I have reviewed the publicly released abstract and attended the oral presentation session. I am, therefore, very knowledgeable about the COBRA study and Reveal's performance in the COBRA study.

V. REVEAL'S PERFORMANCE IN THE COBRA STUDY

A. Phase II Endpoint Analysis

27. The Phase II endpoint analysis leading to the COBRA study's termination was based on an analysis of data from 16-patient sample that tested positive for ctDNA as the baseline out of all of those enrolled.[20] This included 7 patients in the observation arm and 9 in the treatment arm. These patients had their ctDNA levels observed at the six-month time point to determine who had achieved "clearance" (*i.e.*, conversion from ctDNA- positive to negative) at the six-month mark.[21] This is illustrated in the 2024 COBRA Presentation:[22]



28. The Phase II endpoint result showed that 3 out of the 7 patients (43%) in the observation arm had ctDNA clearance without any treatment (suggesting false positives occurred in testing), while only 1 out of 9 patients (11.1%) in the treatment arm had clearance (fewer cases than

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[20] Ex. 2 (2024 COBRA Abstract).
[21] *Id.*
[22] Ex. 1 (2024 COBRA Presentation) at 11.

expected).[23] As I explain below, these results were highly aberrant and demonstrate that the Reveal test did not work as Guardant and Dr. Parikh reported.

29. Generally, a patient who tests positive for ctDNA at the baseline but does not receive any intervening chemotherapy continues to have the microscopic disease that has not been treated. If an MRD test works properly, that same patient should continue to test positive for ctDNA at the six-month mark, because of the untreated disease. On the other hand, at least 40-60% of patients who tests positive for ctDNA at the baseline and receive chemotherapy thereafter are expected to see ctDNA clearance (*i.e.*, test negative for ctDNA) after six months. We know this to be the case because (1) chemotherapy is known to be able to eradicate microscopically present cancer and clear the patients' ctDNA; and (2) the data from other large prospective studies supports these expectations.

30. For instance, in the GALAXY observational trial,[24] approximately 66% of ctDNA-positive patients who received adjuvant chemotherapy achieved clearance.[25] The GALAXY trial is part of the CIRCULATE-Japan trial, which is the largest prospective, multi-center, MRD-guided clinical trial in the CRC field. The GALAXY trial utilizes the Signatera assay.[26] During this year's ASCO-GI, the Japanese investigators reported that 5,781 patients had enrolled in the GALAXY trial, and samples from 2,998 patients were analyzed.[27] Given the size of the GALAXY trial, that observed clearance rate supports a reliable general expectation for the clearance rate for patients who received chemotherapy following testing positive for ctDNA.

31. The results reported by the GALAXY trial are also consistent with the results reported in the U.S. observational "BESPOKE" trial, which also uses Signatera as the ctDNA test.

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[23] *Id.*; Ex. 2 (2024 COBRA Abstract).

[24] I discussed the GALAXY trial in my Opening Report. *See* Op., ¶¶ 79-83.

[25] Ex. 4 (Nakamura et al., *Circulating tumor DNA (ctDNA) dynamics in colorectal cancer (CRC) patients with molecular residual disease: Updated analysis from GALAXY study in the CIRCULATE-JAPAN*, ASCO-GI Presentation Slides (2024) (hereinafter "2024 GALAXY Presentation")) at 6.

[26] *See* Op., ¶¶79-83.

[27] Ex. 4 (2024 GALAXY Presentation) at 2.

Dr. Pashtoon Kasi reported the findings of the BESPOKE trial during ASCO-GI 2024.[28] In the BESPOKE trial, 42.4% of ctDNA-positive patients who received chemotherapy achieved clearance in this trial.[29]

32. The results reported in the COBRA study Phase II endpoint analysis do not meet the established expectations for clearance, which points to issues with Reveal. First, the observation group confirms that there were issues with false positives with the assay. All 7 patients started with ctDNA positive using the Reveal assay. Normally, these 7 patients would be expected to continue to test ctDNA positive at the six-month mark, as it is highly unusual that a ctDNA positive result will convert to ctDNA negative without any treatment intervention. However, as the COBRA study reported, 3 out of 7 patients (43%) converted from ctDNA positive to negative.[30] It is highly improbable that 43% of the patients with positive tests would clear ctDNA without treatment. This result indicates that the three patients who tested negative at the six-month mark should not have been tested positive at the baseline—*i.e.*, their initial ctDNA positive results are false positive results.

33. Conversely, in the 9-patient group that received chemotherapy intervention, only 1 out of 9 patients (11%) achieved clearance at the six-month mark.[31] This, again, does not align with the expectation because, as the large patient population in the GALAXY and BESPOKE trial has shown, the expected clearance for those who received chemotherapy should be in the 40-60% range (or 4-6 patients in this group), far higher than the 11% (1 out of 9 patients) reported by the COBRA study. Unfortunately, at this point, without further recurrence data, we are unable to conclude whether the initial ctDNA results for these 9 patients were false-positive or false-negative.

34. From a statistical point of view, the COBRA study data showed that the Reveal test did not work as Guardant advertised either. As discussed earlier, the p-value goal for this Phase II

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[28] Ex. 5 (Aushev et al., *Circulating tumor DNA (ctDNA) for informing adjuvant chemotherapy (ACT) in stage II/III colorectal cancer (CRC): Interim Analysis of BESPOKE CRC Study*, ASCO-GI Presentation Slides (2024) (hereinafter "2024 BESPOKE Presentation")) at 1.

[29] *Id.* at 6

[30] Ex. 1 (2024 COBRA Presentation) at 11; Ex. 2 (2024 COBRA Abstract).

[31] Ex. 1 (2024 COBRA Presentation) at 11; Ex. 2 (2024 COBRA Abstract).

endpoint analysis is $p<0.35$, which is already significantly more permissive than the usual $p<0.05$ standard. But Reveal's performance is so far away from even that lowered standard. The reported p-value is 0.98,[32] which effectively means that, with respect to the endpoint of "ctDNA clearance," Reveal only has a 2% chance of accurately predicting DNA clearance. In other words, Reveal was unable to distinguish between positive patients treated with chemotherapy or those observed without chemotherapy.

35. Regardless, the aberrant results from these 16 patients confirm that Reveal was not performing as reported by Guardant and Parikh. These false calls rendered the COBRA study meaningless. While clinical trials do fail on occasion, the failure of this magnitude is unheard of and will have tremendous and long-lasting impacts on the field.

B. Impact of Reveal's Performance in the COBRA Study

36. Guardant Reveal's performance in the COBRA study is disappointing to say the least, especially given the scale of the COBRA study—a massive national trial with more than 400 sites nationwide—and at the cost of thousands of person-hours of effort by the physicians and medical research staff at the NRG, the NCI, and all the participating sites who initiated the trial and then conducted the study at those approximately 400 treatment sites nationwide, not to mention the millions of dollars of government funding required to sustain the trial for four years.

37. Upon announcing the halt of the COBRA Study, NRG Oncology supplied letters to trial investigators to share with patients involved in the study, citing a greater-than-expected false positive rate.[33] The August 30, 2023 letter that I received stated:[34]

[32] Ex. 2 (2024 COBRA Abstract).

[33] *See* Ex. 6 (Molika Ashford, *Trial Failure Raises Questions About MRD Testing Utility, but Prognostic Evidence Remains Strong*, GENOMEWEB (Jan. 26, 2024) https://www.genomeweb.com/molecular-diagnostics/trial-failure-raises-questions-about-mrd-testing-utility-prognostic-evidence).

[34] Attached as Exhibit 7.

NRG ONCOLOGY

Advancing Research. Improving Lives.™

NRG-GI005

Phase II/III Study of Circulating tumOr DNA as a Predictive BiomaRker in Adjuvant Chemotherapy in Patients with Stage IIA Colon Cancer (COBRA)

August 30, 2023

Dear Colleagues:

Thank you for your support of the NRG-GI005 phase II/III trial evaluating circulating tumor DNA (ctDNA) as a predictive biomarker for benefit of adjuvant chemotherapy for patients with resected, stage IIA colon cancer. We are conducting our prospectively planned interim analysis for the phase II endpoint of this study (i.e., to determine the rate of ctDNA clearance following chemotherapy). We have been informed by our diagnostic partner that a greater than anticipated number of participants may have been "false positives", i.e., designated ctDNA+ incorrectly. While this was a recognized potential risk of the study, this rate is higher than we had expected. Thus, a subset of COBRA patients randomized to Group 2 who tested positive for ctDNA received chemotherapy based on what is potentially a "false positive" result. The higher-than-expected "false positive" rate resulted in the trial not passing the interim analysis and, as such, the trial will be closed to accrual.

38. These are precisely the concerns I expressed in my Opening Report about unreliable, inaccurate ctDNA tests and the harm they bring to patients and the oncology community.[35]

39. As I discussed in my Opening Report, delivering inaccurate results to patients can and will have long-lasting and devastating impacts on the patients.[36] For example, patients may be forced to go through additional confirmatory tests (if receiving a false-positive result) or suffer unanticipated progressive but undetected cancer (if received a false-negative test).[37] Furthermore, there is considerable emotional turmoil involved in receiving a false result. And inaccurate tests pose significant dilemmas to physicians and have the potential to drive up healthcare costs.[38]

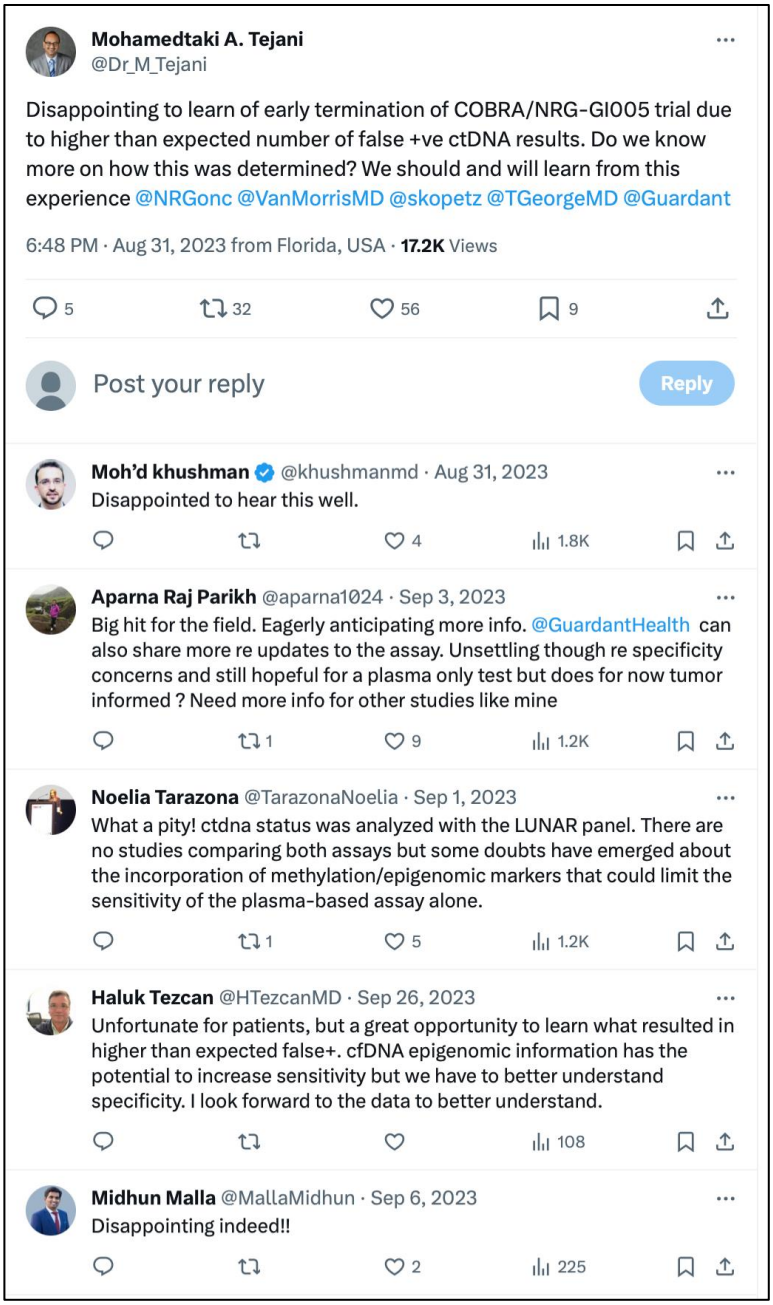
[35] Op., ¶¶ 94-96.
[36] *Id.*, ¶ 96.
[37] *Id.*
[38] *See id.*

VI. REACTIONS FROM THE ONCOLOGY COMMUNITY FOLLOWING THE COBRA STUDY RESULTS

40. Recognizing the consequences of the reported data, the oncology and scientific community raised concerns about the Reveal assay specificity following the COBRA announcement.

41. Physicians publicly aired their disappointment on social media platforms. For example, Dr. Mohamedtaki A. Tejani, an oncologist/hematologist at AdventHealth Medical Group Oncology & Hematology at Orlando, posted his reaction on social media (below).[39] Dr. Tejani's comment is consistent with my concerns about the test and false positives, as expressed in my Opening Report.

[39] https://twitter.com/Dr_M_Tejani/status/1697426196642873710 (last visited Jan. 31, 2024).



42. As shown above, Dr. Parikh replied to that post and also expressed concerns regarding Reveal's specificity. Dr. Parikh posted on her social media account: "Big hit for the field. Eagerly anticipating more info. @GuardantHelth can also share more re updates to the assay. Unsettling though re specificity concerns and still hopeful for a plasma only test . . . ."

43. Dr. Van Morris from MD Anderson—the COBRA Principal Investigator and presenter at ASCO-GI—reflected on these unexpected results in the Abstract for his 2024 ASCO-

GI presentation, stating that "[f]uture trials evaluating ctDNA as an integral biomarker for minimal residual disease determination ***must account for assay specificity*** in this [patient] population."[40]

44. During the Q&A session following his January 20, 2024, presentation at ASCO-GI, Dr. Morris, the lead author of the COBRA study, also expressed that he was disappointed at the results of the COBRA study, "We are every bit as surprised and frankly disappointed by these results."[41] GenomeWeb, a website that reports on biotechnology news, called the results a "disappointing outcome." I share the disappointment expressed by Dr. Tejani, Dr. Parikh, Dr. Morris, and others.

45. The COBRA study's results compounded the concerns regarding the claims of tumor-naïve (non-informed) tests that Guardant made. In an article published on ASCO Daily on January 4, 2024, Dr. Ahmet Ozluk, oncologist at The Ege University School of Medicine in Izmir, Turkey, and Dr. Midhun Malla, professor of medicine at the University of Alabama at Birmingham, wrote for the ASCO Daily News that "[a]lthough both tumor-informed and -uninformed assays are available commercially, tumor-informed assay seems to have stronger data, with the availability of larger datasets to date, as well as improved sensitivity and specificity of the assay."[42] This is consistent with my opinions set forth in my Opening Report.

46. Guardant Reveal's poor performance in the COBRA study further reinforced my concerns regarding the test, as set forth in my Opening Report and Rebuttal Report.[43] Though the data presented in the Parikh Study, and advertised by Guardant, may have represented Reveal to be comparable to tumor-informed test, when battle-tested in a real-world setting via a prospective,

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[40] Ex. 2 (2024 COBRA Abstract) (emphasis added).

[41] Ex. 6 (GenomeWeb Article)

[42] Ozluk & Malla, *Personalizing Adjuvant Treatment Using ctDNA in Colon Cancer*, ASCO DAILY NEWS (Jan. 4, 2024), https://dailynews.ascopubs.org/do/personalizing-adjuvant-treatment-using-ctdna-colon-cancer#:~:text=Although%20both%20tumor%2Dinformed%20and,and%20specificity%20of%20the%20assay; *see also*, *id.* ("Unfortunately, the COBRA study (NCT04068103) has been terminated because of higher-than-expected false-positive ctDNA results with tumor-agnostic assay, ***likely attributed to methylation and epigenomic markers*** that could have limited the sensitivity of the assay.") (emphasis added).

[43] Op., ¶¶ 89, 94-96.; *see also* Reb., ¶¶ 10-13.

randomized trial like COBRA, conducted by an independent sponsor, with no room for manipulation, the true performance of Reveal, as exposed, is too prone to aberrant results, cannot meet expectations, and is not on par with tumor-informed tests.

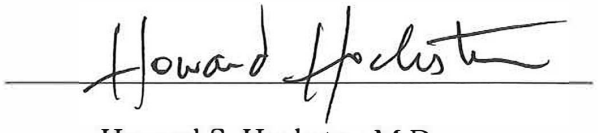
VII. CONCLUSION

47. My opinions are subject to change based on additional opinions that Guardant's experts may present and information I may receive in the future or additional work I may perform. With this in mind, based on the analysis I have conducted and for the reasons set forth above, I have reached the conclusions and opinions in this report.

48. In connection with my anticipated testimony in this action, I may use as exhibits various documents produced in this case that refer to or relate to the matters discussed in this report, my Opening Report, and my Rebuttal Report. I have not yet selected the particular exhibits that might be used. In addition, I may create or assist in the creation of certain demonstrative evidence to assist me in testifying, and I reserve the right to do so, such as videos or other multimedia material, to further support the positions in this report.

49. At hearings and at trial, and as discussed above, I may rely on visual aids and analogies concerning the issues and technologies implicated in this case.

Executed this 31st day of January, 2024.



Howard S. Hochster, M.D.